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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,907	05/29/2001	Andrew Raymon Morton Bradbury	DSP/HB/07.01US	6402

7590 02/02/2009

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EXAMINER	
LUNDGREN, JEFFREY S	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
02/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/856,907	BRADBURY ET AL.	
	Examiner	Art Unit	
	JEFFREY S. LUNDGREN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44 46-92* is/are pending in the application.

4a) Of the above claim(s) *3 and 19-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-44 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-44, 46-92 are pending in the instant application; claims 3 and 19-92 are withdrawn as being directed to non-elected inventions; claims 1, 2, 4-44 and 46-48 are the subject of the Office Action below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-44 and 46-48 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and each of the dependent claims are indefinite for reciting the phrase "*essentially every* members" because one of ordinary skill in the art could not reasonable determine the metes and bounds of this limitation. This phrase is one of relative nature or degree, and precludes a reasonable determination as to the quantity of members that are include within the scope of the claim and the quantity of members that are not included within the scope of the claim. Correction is required.

Claim 1 and each of the dependent claims are indefinite for reciting the phrase "an identical vector backbone sequence" because one of ordinary skill in the art could not reasonable determine the metes and bounds of this limitation. It is not clear from any part of the file wrapper if the "sequence" length has a cutoff or a definitive endpoint, such as, two sequences having identical sequences of a span of two (2) nucleotides. The phrase is not a definitive term of art, nor is there sufficient guidance in the specification for determining, for example, the length of "vector backbone" or the genetic elements required to constitute a "backbone."

Claim Rejections - 35 USC § 112 – New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-44 and 46-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the introduction of new matter. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the specification does not have adequate support for the phrases "essentially every member" and "an identical vector backbone sequence," either literally or *via* means of example. Applicants allege in their reply that support for their amendments can be found in the specification as originally filed, such as, at page 5, lines 4-7; page 20, lines 7-11 and 28-30; page 22, line 23, and page 26, lines 5-14 and 23-27. However, a review of these portions of the specification neither literally, nor with reasonable interpretation suggest the disputed claim limitations.

Claim Rejections - 35 USC § 102—Maintained

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claims 1, 2, 4-44 and 46-48 as anticipated by Johnson:

The rejection of claims 1, 2, 4-44 and 46-48, under 35 U.S.C. § 102(b) as being anticipated by Johnson *et al.*, U.S. Patent No. 5,733,743, issued March 31, 1998, is maintained.

Claim 1 is directed to a method of preparing a nucleic acid library, said method comprising introducing at least two members of an initial population of nucleic acid molecules into at least one cell, wherein essentially every member of the initial population of nucleic acid molecules comprises an identical vector backbone; and a nucleic acid sequence that varies

between members of said population and which comprises a substrate for recombination, said introducing resulting in recombination of said substrate for recombination between at least two members of the population thereby producing a population comprising recombined nucleic acid members. Claim 48 is directed to a library of nucleic acids for the purpose of claim.

Johnson teaches methods for the production of members of specific binding pairs (sbp), *e.g.*, antibodies, using display on the surface of secreted replicable genetic display packages (rgdps), *e.g.*, filamentous phage, via certain host cells. To produce a library of great diversity, recombination occurs between first and second vectors comprising nucleic acids encoding first and second polypeptide chains of sbp members respectively, thereby producing recombinant vectors each encoding both a first and a second polypeptide chain component of an sbp member. The recombination may take place in vitro or intracellularly and may be site-specific, e.g. involving use of the loxP sequence and mutants thereof. Recombination may take place after prior screening or selecting for rgdps displaying sbp members which bind complementary sbp member of interest (see Figs. 3A and 3B, and description thereof). As shown in Figs 3A and 3B, both nucleic acid members are introduced to the cell. Accordingly, claims 1 and 48 are anticipated. The fact that Johnson teaches segments that have some identity, meets the limitation "an identical vector backbone sequence" as the backbone sequence only needs to be two nucleotides in length.

As in claims 2 and 4-10, Johnson teaches the use of various recombination mechanisms for creating the library; Johnson states:

> "***Another way of enriching for productive recombination events is to employ mutant loxP sites. Several mutants of the loxP sequence are known, and these are compromised with respect to their ability to recombine with each other and the wild-type loxP sequence*** (Hoess, R. H., Wierzbicki, A. and Abremski, K. (1986) Nucl. Acids Res. 14, 2287-2300). For example, ***loxP 511*** has a G→A point mutation in the central 8 bp segement, with the result that it will only recombine with other loxP 511 sites, but not the wild-type loxP sequence (Hoess, R. H., Wierzbicki, A. and Abremski, K. (1986) et supra.). Placement of ***wild-type and mutant loxP sequence combinations can direct which recombination events are possible: their use is described in example 1***. Other mutant loxP sites are known but their abilities to recombine with each other and the wild-type loxP sequence have not been extensively characterised, presumably loxP 511 is not unique. ***Provision of different mutant loxP***

> ***sites in the vectors would permit even greater control over the occurance of recombination events perhaps leading to more complex, controllable and efficient recombination strategies being possible***."

Johnson, paragraph bridging cols. 16 and 17 (emphasis added). Accordingly, claims 11-13 are anticipated.

As in claim 14-23, Johnson teaches a range of reagents for delivering the nucleic acid library members, such as the phage:

> "In one embodiment, [t]he recombination is intracellular and takes place in a ***bacterial host*** which replicates the recombinant vector preferentially over the first vectors and the second vectors. This may be used to enrich selection of successful recombination events. The intracellular recombination may take place in a bacterial host which replicates plasmids preferentially over phages or phagemids, or which replicates phages or phagemids preferentially over plasmids. For instance, the bacterial host may be a PolA strain of ***E. coli*** or of another gram-negative bacterium. PolA cells are unable to support replication of plasmids, but can support replication of ***filamentous phage and phagemids (plasmids containing filamentous phage intergenic regions)***. So, for instance, if the first vectors are plasmids containing a first marker gene, and the second vectors are phage or phagemids containing a second marker gene, selection for both markers will yield recombinant vectors which are the product of a successful recombination event, since recombination transferring the first marker from plasmid must take place in order for that marker to be replicated and expressed."

Johnson, col. 12, lines 42-61; and previously where Johnson states:

> "The particle may be a virus e.g. a bacteriophage such as ***fd or M13*** **[i.e., a Ff family phage member]**."

Johnson, col. 7, lines 59 and 60 (emphasis added). Accordingly, the claim limitation of claim 25, 35, 38 and 43, are met by the aforementioned paragraphs.

The expression cassette limitation of claim 26 is met by Figs. 3A and 3B and the corresponding description (see above). As in claim 27, one or more polypeptides are encoded for; as in claim 28, the encoded polypeptides are flanked by the recombination sites (see Figs. 3A

and 3B and the corresponding description). As noted above, the limitations of phage, phagemid and bacterium polypeptide expression in claim 29, 34, 36 and 37, are all taught by Johnson.

As also noted above, the specific binding pair limitations of claim 30 are met by the variable chain (light and heavy) teaching in Johnson, where Johnson teaches the recombined antibodies (see above), as in claims 31, 39 and 40 (*i.e.*, scFv; Johnson col. 1, lines 52-59; see also Johnson, col. 8, lines 1-7). Regarding claims 32 and 33, Johnson teaches CDR3 and the VH and VL regions of the polypeptide (see Example 1; also see Figs. 3A and 3B and the corresponding description). As in claim 42, Johnson discloses a polypeptide linker comprising a recombination site of the V region (Figs. 3A and 3B and the corresponding description). Regarding claims 44-47, Johnson teaches:

> "So, for instance, if the ***first vectors are plasmids containing a first marker gene, and the second vectors are phage or phagemids containing a second*** marker gene, selection for both markers will yield recombinant vectors which are the product of a successful recombination event, since recombination transferring the first marker from plasmid must take place ***in order for that marker to be replicated and expressed***."

Johnson, col. 12, lines 54-61 (emphasis added).

Accordingly, the rejection is maintained.

Conclusions

No claim is allowable.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey S. Lundgren/
Patent Examiner, Art Unit 1639